

What is claimed is

1. A method of prophylaxis of a disease associated with amyloid deposits of A β in the brain of a patient, comprising administering an effective regime of a fragment of A β , wherein the fragment induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43 without inducing antibodies that specifically bind to one or more epitopes between residues 1-11, and the fragment is not A β 13-28, 17-28, 25-35, 35-40, 33-42 or 35-42, whereby the induced antibodies specifically bind to soluble A β in the patient thereby inhibiting formation of amyloid deposits of A β in the brain from the soluble A β , and thereby effecting prophylaxis of the disease

2. The method of claim 1, wherein the fragment is free of an intact T-cell epitope that induces a T-cell response to A β .

3. The method of claim 1, wherein the induced antibodies lack capacity to specifically bind to amyloid deposits of A β .

4. The method of claim 1, wherein the fragment contains a segment of 5-10 contiguous amino acids of A β .

5. The method of claim 1, wherein the fragment contains a segment of 5-10 contiguous amino acids within A β 15-24.

6. The method of claim 1, wherein the fragment is selected from the group consisting of A β 15-21, A β 16-22, A β 17-23, A β 18-24, A β 19-25, A β 15-22, A β 16-23, A β 17-24, A β 18-25, A β 15-23, A β 16-24, A β 17-25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25.

7. The method of claim 1, wherein the fragment is a C-terminal fragment that induces antibodies that specifically bind to A β 42 and/or A β 43 without specifically binding to A β 39, 40 or 41.

8. A method of prophylaxis of a disease associated with amyloid deposits of A β in the brain of a patient, comprising administering an effective regime of a fragment of A β , wherein the fragment is selected from the group consisting of A β 15-21, A β 16-22, A β 17-23, A β 18-24, A β 19-25, A β 15-22, A β 16-23, A β 17-24, A β 18-25, A β 15-23, A β 16-24, A β 17-25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25.

25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25, and thereby effect prophylaxis of the disease.

9. The method of claim 1, method further comprising administering a fragment of A β that induces antibodies specifically binding to A β at one or more epitopes with A β 1-11.

10. The method of claim 9, wherein the fragment of A β that induces antibodies specifically binding to A β at an epitope with A β 1-11 is administered before the fragment induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43.

11. The method of claim 1, further comprising administering an antibody that specifically binds to A β at an epitope with A β 1-11.

12. The method of claim 1, wherein the antibody that specifically binds to A β at an epitope with A β 1-11 is administered before the fragment that induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43.

13. The method of claim any of the preceding claims, wherein the disease is characterized by cognitive impairment.

14. The method of claim any of the preceding claims, wherein the disease is Alzheimer's disease.

15. The method of claim any of the preceding claims, wherein the disease is Down's syndrome.

16. The method of claim any of the preceding claims, wherein the disease is mild cognitive impairment.

17. The method of any of the preceding claims, wherein the patient is human.

18. The method of any of the preceding claims, further comprising monitoring the induced antibodies in the patient.

19. The method of any of the preceding claims, wherein the patient is asymptomatic.
20. The method of any of the preceding claims, wherein the patient is symptomatic and the administering inhibits deterioration of the patient's symptoms.
21. The method of any of the preceding claims, wherein the patient is under 50.
22. The method of any of the preceding claims, wherein the patient has an inherited risk factor indicating susceptibility to Alzheimer's disease.
23. The method of claim 19, wherein the patient does not develop detectable symptoms for five years after the administering step is first performed.
24. The method of any of claims 1-21 and 23, wherein the patient has no known risk factors for Alzheimer's disease.
25. The method of any of the preceding claims, wherein the regime comprises administering a dosage of at least 50 micrograms of the fragment on a plurality of days.
26. The method of any of the preceding claims, wherein the fragment is administered with an adjuvant that increases the level of antibodies induced by the fragment.
27. The method of any of the preceding claims, wherein the fragment is administered intraperitoneally, orally, intranasally, subcutaneously, intramuscularly, topically or intravenously.
28. The method of any of the preceding claims, wherein the fragment is administered by administering a polynucleotide encoding the fragment, wherein the polynucleotide is expressed to produce the fragment in the patient.
29. The method of any of the preceding claims, further comprising monitoring the patient for level of induced antibodies in the blood of the patient.
30. The method of any of the preceding claims, wherein the fragment is administered in multiple dosages over a period of at least three months.

31. The method of claim 30, wherein the dosages are at least 50 micrograms.
32. The method of claim 1, wherein the fragment is linked to a carrier molecule to form a conjugate.
33. The method of any of claim 32, wherein the carrier is a heterologous polypeptide.
34. The method of claim 32, wherein multiple copies of the fragment are linked to a carrier molecule to form a conjugate.
35. The method of claim 32, wherein multiple copies of the fragment are linked to multiple copies of the carrier molecule, which are linked to each other.
36. The method of claim 33, wherein the heterologous polypeptide comprises QYIKANSKFIGITEL (SEQ ID NO:8).
37. The method of claim 33, wherein the heterologous polypeptide comprises the amino acid sequence AKXVAAWTLKAAA (SEQ ID NO11).
38. The method of claim 33, wherein the polypeptide induces a T-cell response against the heterologous polypeptide and thereby a B-cell response against the fragment.
39. The method of claim 1, further comprising administering an adjuvant that enhances the titer and/or binding affinity of the induced antibodies relative to administering the fragment alone.
40. The method of claim 39, wherein the adjuvant and the polypeptide are administered together as a composition.
41. The method of claim 39, wherein the adjuvant is administered before the polypeptide.
42. The method of claim 39, wherein the adjuvant is administered after the polypeptide.
43. The method of claim 39, wherein the adjuvant is alum.

44. The method of claim 39, wherein the adjuvant is MPL.
45. The method of claim 39, wherein the adjuvant is QS-21.
46. The method of claim 39, wherein the adjuvant is incomplete Freund's adjuvant.

47. The method of any of the preceding claims, wherein the dosage of the fragment is greater than 10 micrograms.

48. A method of treating a disease associated with amyloid deposits of A β in the brain of a patient, comprising administering an effective regime of a fragment of A β , wherein the fragment induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43 without inducing antibodies that specifically bind to one or more epitopes between residues 1-11, and the fragment, 33-42 A β 13-28, 17-28, 25-35, 35-40 or 35-42, whereby the induced antibodies specifically bind to soluble A β in the patient thereby inhibiting formation of amyloid deposits of A β in the brain from the soluble A β , and thereby treat the disease.

49. The method of claim 48, wherein the fragment is free of an intact T-cell epitope that induces a T-cell response to A β .

50. The method of claim 48, wherein the induced antibodies lack capacity to specifically bind to amyloid deposits of A β .

51. The method of claim 48, wherein the fragment contains a segment of 5-10 contiguous amino acids of A β .

52. The method of claim 48, wherein the fragment contains a segment of 5-10 contiguous amino acids within A β 15-24.

53. The method of claim 48, wherein the fragment is selected from the group consisting of A β 15-21, A β 16-22, A β 17-23, A β 18-24, A β 19-25, A β 15-22, A β 16-23, A β 17-24, A β 18-25, A β 15-23, A β 16-24, A β 17-25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25.

54. The method of claim 48, wherein the fragment is a C-terminal fragment that induces antibodies that specifically bind to A β 42 and/or A β 43 without specifically binding to A β 39, 40 or 41.

55. A method of treating a disease associated with amyloid deposits of A β in the brain of a patient, comprising administering an effective regime of a fragment of A β , wherein the fragment is selected from the group consisting of A β 15-21, A β 16-22, A β 17-23, A β 18-24, A β 19-25, A β 15-22, A β 16-23, A β 17-24, A β 18-25, A β 15-23, A β 16-24, A β 17-25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25, and thereby treat the disease.

56. The method of claim 55, method further comprising administering a fragment of A β that induces antibodies specifically binding to A β at one or more epitopes with A β 1-11.

57. The method of claim 56, wherein the fragment of A β that induces antibodies specifically binding to A β at an epitope with A β 1-11 is administered before the fragment induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43.

58. The method of claim 48, further comprising administering an antibody that specifically binds to A β at an epitope with A β 1-11.

59. The method of claim 48, wherein the antibody that specifically binds to A β at an epitope with A β 1-11 is administered before the fragment that induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43.

60. The method of claim any of the preceding claims, wherein the disease is characterized by cognitive impairment.

61. The method of claim any of the preceding claims, wherein the disease is Alzheimer's disease.

62. The method of claim any of the preceding claims, wherein the disease is Down's syndrome.

63. The method of claim any of the preceding claims, wherein the disease is mild cognitive impairment.

64. The method of any of the preceding claims, wherein the patient is human.

65. The method of any of the preceding claims, further comprising monitoring the induced antibodies in the patient.

66. The method of any of the preceding claims, wherein the patient is asymptomatic.

67. The method of any of the preceding claims, wherein the patient is symptomatic and the administering inhibits deterioration of the patient's symptoms.

68. The method of any of the preceding claims, wherein the patient is under 50.

69. The method of any of the preceding claims, wherein the patient has an inherited risk factor indicating susceptibility to Alzheimer's disease.

70. The method of claim 66, wherein the patient does not develop detectable symptoms for five years after the administering step is first performed.

71. The method of any of claims 1-68 and 70, wherein the patient has no known risk factors for Alzheimer's disease.

72. The method of any of the preceding claims, wherein the regime comprises administering a dosage of at least 50 micrograms of the fragment on a plurality of days.

73. The method of any of the preceding claims, wherein the fragment is administered with an adjuvant that increases the level of antibodies induced by the fragment.

74. The method of any of the preceding claims, wherein the fragment is administered intraperitoneally, orally, intranasally, subcutaneously, intramuscularly, topically or intravenously.

75. The method of any of the preceding claims, wherein the fragment is administered by administering a polynucleotide encoding the fragment, wherein the polynucleotide is expressed to produce the fragment in the patient.

76. The method of any of the preceding claims, further comprising monitoring the patient for level of induced antibodies in the blood of the patient.

77. The method of any of the preceding claims, wherein the fragment is administered in multiple dosages over a period of at least three months.

78. The method of claim 77, wherein the dosages are at least 50 micrograms.

79. The method of claim 55, wherein the fragment is linked to a carrier to form a conjugate.

80. The method of any of claim 79, wherein the carrier is a heterologous polypeptide.

81. The method of claim 79, wherein multiple copies of the fragment are linked to a carrier to form a conjugate.

82. The method of 79, wherein multiple copies of the fragment are linked to multiple copies of the carrier, which are linked to each other.

83. The method of claim 80, wherein the heterologous polypeptide comprises QYIKANSKFIGITEL (SEQ ID NO:8).

84. The method of claim 80, wherein the heterologous polypeptide comprises the amino acid sequence AKXVAAWTLKAAA (SEQ ID NO:11).

85. The method of claim 80, wherein the polypeptide induces a T-cell response against the heterologous polypeptide and thereby a B-cell response against the fragment.

86. The method of claim 55, further comprising administering an adjuvant that enhances the titer and/or binding affinity of the induced antibodies relative to administering the fragment alone.

87. The method of claim 86, wherein the adjuvant and the polypeptide are administered together as a composition.

88. The method of claim 86, wherein the adjuvant is administered before the polypeptide.

89. The method of claim 86, wherein the adjuvant is administered after the polypeptide.

90. The method of claim 86, wherein the adjuvant is alum.

91. The method of claim 86, wherein the adjuvant is MPL.

92. The method of claim 86, wherein the adjuvant is QS-21.

93. The method of claim 86, wherein the adjuvant is incomplete Freund's adjuvant.

94. The method of any of the preceding claims, wherein the dosage of the fragment is greater than 10 micrograms.

95. A pharmaceutical composition comprising a fragment of A β as defined in any of claims 48-55 and an adjuvant.

96. The use of a fragment of A β effective to treat or effect prophylaxis of a disease associated with amyloid deposits of A β in the brain of a patient in the manufacture of a medicament, wherein the A β fragment induces antibodies that specifically bind to A β at one or more epitopes between residues 12 and 43 without inducing antibodies that specifically bind to one or more epitopes between residues 1-11, and the fragment is not A β 13-28, 17-28, 25-35, 35-40 or 35-42, whereby the induced antibodies specifically bind to soluble A β in the patient thereby inhibiting formation of amyloid deposits of A β in the brain from the soluble A β , and thereby effecting prophylaxis of the disease.

97. The use of claim 96, wherein the fragment is free of an intact T-cell epitope that induces a T-cell response to A β .

98. The use of claim 96, wherein the induced antibodies lack capacity to specifically bind to amyloid deposits of A β .

99. The use of claim 96, wherein the fragment contains a segment of 5-10 contiguous amino acids of A β .

100. The use of claim 96, wherein the fragment contains a segment of 5-10 contiguous amino acids within A β 15-24.

101. The use of claim 96, wherein the fragment is selected from the group consisting of A β 15-21, A β 16-22, A β 17-23, A β 18-24, A β 19-25, A β 15-22, A β 16-23, A β 17-24, A β 18-25, A β 15-23, A β 16-24, A β 17-25, A β 18-26, A β 15-24, A β 16-25, and A β 15-25.

102. The use of claim 96, wherein the fragment is a C-terminal fragment that induces antibodies that specifically bind to A β 42 and/or A β 43 without specifically binding to A β 39, 40 or 41.